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10/559,385	06/21/2006	Werner Mederski	MERCK-3107	5930

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EXAMINER	
ANDERSON, REBECCA L	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
12/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/559,385	MEDERSKI ET AL.	
	Examiner	Art Unit	
	REBECCA L. ANDERSON	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-4,6,7,9-12 and 14* is/are allowed.

6)☒ Claim(s) *5,13 and 15-17* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-17 are currently pending in the instant application. Claims 1-4, 6, 7, 9-12 and 14 appear allowable over the prior art of record. Claims 5, 13 and 15-17 are rejected. Claim 8 is objected.

Response to Amendment and Arguments

Applicant's amendment and arguments filed 26 August 2009 have been fully considered and entered into the instant application. Applicants' amendment has overcome the objection to claim 6. Applicants' amendment to claims 13 and 15 has overcome the rejection under 35 USC 101. Applicants' amendment has overcome the 35 USC 112 1st paragraph rejection in regards to "solvates" and "derivative" in all but claim 5 wherein this language is still present. Therefore, the 35 USC 112 1st paragraph rejection of claim 5 is maintained.

In regards to the 35 USC 112 1st paragraph rejection of claims 13 and 15, applicants' arguments have been considered but they are not persuasive. Therefore, the 35 USC 112 1st paragraph rejection is maintained and newly added claims 16 and 17 are also rejected.

Applicants argue that the breadth of the claims is not seen to be relevant to enablement of the claims and that the discussion on pages 2-4 is sufficient to establish utility of the application for purposes of the 112 statute and that an unsupported suggestion that the method would not work is insufficient basis alone for rejecting the claims. This argument is not persuasive as the examiner has not just stated that the instant claims are not enabled, but has also provided references to support that the

instant claims are not enabled as can be seen by the references provided in the 35 USC 112 1st paragraph rejection.

Applicants argue that the Examiner has not provided any such reasons or evidence to doubt the assertion of utility in the specification and that the mere breadth of the claims does not, without more, result in non-enablement. This argument is not persuasive as the examiner has provided multiple references to support the reasons to doubt the assertion of utility in the specification. Specifically, the examiner has cited Golub et al, Lala et al., Kaiser and Hauptmann et al. which support the non-enablement of the claims as the state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531) Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are

different cellular mechanisms, the unpredictability in the art and the different treatment protocols. Additionally, for the newly added claims, the lack of predictability in the art of applicants' invention can be seen for example, in that it is the state of the art that data on the metabolism of factor Xa inhibitors has not been published yet (Hauptmann et al., page 223, 1449 page 6) and at the time of the publication, no published reports on the clinical use of factor Xa inhibitors existed. Furthermore, as seen in Kaiser (1449, page 6), Most of the specific factor Xa inhibitors known at the time of publication are still in the phase of preclinical development or are being investigated in first clinical studies, and while many treatment possibilities are discussed as possibilities, the real potential of factor Xa inhibitors has still to be validated in comprehensive clinical trials. Furthermore, an important point is that factor Xa inhibitors cannot interrupt thrombotic processes which are caused by generated thrombin. Page 432 of Kaiser states that Despite major progress in the development of antifactor Xa agents, there are still some unresolved issues such as that they are expected to be much less antithrombotically effective when sufficient amounts of thrombin have already been generated. Kaiser also discloses on page 433 that A particular factor Xa inhibitor might be useful for only a specific clinical indication, and it is likely that one drug might not be the optimum treatment for all thrombotic situations.

Applicants also argue that it is not necessary for Applicants' method claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods, are interpreted to be per se functional. This argument is not persuasive as it would be undue

experimentation for one of ordinary skill in the art to determine the scope of the claims as the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. Additionally, it would require undue experimentation to determine what compounds could treat what diseases when faced with the prior art references that provide for the lack of predictability in the art.

While applicants argue that pharmacological data is given in the instant specification on page 21 to show inhibition activity on factor Xa, again it is noted that applicant has not provided any correlation to the treatment of any disease. The only direction or guidance present in the instant specification is the listing of diseases applicant considers as treatable on pages 4 and 5. In vitro data is discussed on page 21. However, the disclosure does not provide how the in vitro data correlates to the treatment of the assorted diseases claimed.

The uses covered by the claims are not enabled based solely on the assay testing reported in the specification. Various studies reported for compounds in clinical development rely on animal models and not simply assay testing as done herein. Note Hoffman V. Klaus 9 USPQ2d 1657 regarding the standard of testing that is necessary to establish the likelihood of in vivo use. Also see Ex parte Powers 220 USPQ 925. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of in vivo efficacy by those skilled in the art. See for example, In re Ruskin 148 USPQ 221; Ex parte Jovanovics 211 USPQ 907. Any evidence relied on by

applicants must clearly show a reasonable expectation of in vivo success for any additional diseases that may still be embraced in response to this action. See MPEP 2164.05(a).

Additionally, for example, in regards to the treatment of specific cancers, in general, cell culture studies are not considered, in the cancer arts, to be reliably predictive of effects in cancer treatment, in vitro assays cannot easily assess host-tumor and cell-cell interactions that may be important in the malignant state and cannot duplicate the complex conditions of in vivo therapy. This is because characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Those of skill in the art recognize that *in vitro* assays are useful to screen the effects of agents on cells. However, clinical correlations are generally lacking. The greatly increased complexity of the *in vivo* environment as compared with the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a simple extrapolation of *in vitro* assays to human therapeutic efficacy with any reasonable degree of predictability.

Further, there is no disclosure regarding how all types of diseases claimed having divers mechanisms are treated. Receptor activity is generally unpredictable and a highly structure specific area, and the data provided of is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Lastly, Applicants argue that the noted inhibitors are well known to be implicated in signaling pathways which are instrumental in the formation of tumors and that the testing of each type of tumor is routine. This argument is not persuasive as the uses covered by the claims are not enabled based solely on the assay testing reported in the specification. Various studies reported for compounds in clinical development rely on animal models and not simply assay testing as done herein. Note Hoffman V. Klaus 9 USPQ2d 1657 regarding the standard of testing that is necessary to establish the likelihood of in vivo use. Also see Ex parte Powers 220 USPQ 925. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of in vivo efficacy by those skilled

in the art. Additionally, This argument is not persuasive as the examiner has provided multiple references to support the reasons to doubt the assertion of utility in the specification. Specifically, the examiner has cited Golub et al, Lala et al., Kaiser and Hauptmann et al. which support the non-enablement of the claims.

Therefore, the 35 USC 112 1st paragraph rejection of claims 13, 15 and newly added claims 16 and 17 is maintained.

Claim Objections

Claim 8 is objected to because of the following informalities: Specifically, claim 8 as amended now reads :Process for the preparation of compounds of the formula I according to claim 1 or pharmaceutically usable ***comprising*** salts or stereoisomers thereof, comprising…" It is suggested that the first instance of "comprising" be deleted from the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first

paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the products of the formula I and pharmaceutically usable salts and stereoisomers thereof does not reasonably provide enablement for the derivatives and solvates thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with this claim.

The nature of the invention

In the instant case, the claim is read as products of products of the formula I and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof.

The state of the prior art and the predictability or lack thereof in the art

In regards to solvates and hydrates, according to Byrn, et al., "the occurrence of hydrated or solvated crystal forms, crystals in which solvent molecules occupy regular positions in the crystal structure, is widespread but *by no means universal among drug substances*." (emphasis added). Byrn, et al. "Solid State Chemistry of Drugs", 2d ed., SSCI, Inc., Ch. 10 Polymorphs, pp. 232-247, 232 (1999). Most drug crystals that fall into the category of solvates are hydrates. *Id.* at 236.

While the level of skill in pharmacology and organic chemistry is exceedingly high, there is no absolute predictability as to which solvates will function as intended. Byrn notes that the water molecule is particularly suited to fill structural voids, due to its small size. *Id*. In hydrated crystal structures, water molecules bind to other water molecules but also to any available functional group, i.e. carbonyls, amines, alcohols, and many others which are capable of accepting or donating an active hydrogen atom to form hydrogen bonds. *Id*. Also, the behavior of hydrates of pharmaceuticals is unpredictable due to dehydration prior to melting, and cracking during dehydration. *Id*. at 234. Too, hydrates and solvates may only be formed under certain conditions, dependent upon the compounds sought to be crystallized. Such a process is not a given in pharmacology and requires a great deal of research, with no guarantee of success.

Furthermore, the stability of solvates and hydrates is not altogether predictable, wherein said stability directly affects the properties of a given molecule. This lack of stability means a hydrate or solvate, if found to possess similar properties as the target compound, may not function as intended *in vivo*. Such facts lead to the conclusion that more that a mere recitation is needed in order to support a claim to solvates and hydrates. Creating functional solvates and hydrates with the same properties as the mother-compound is by no means routine, thus there must be a showing sufficient to satisfy the enablement requirement.

The state of the prior art is that the term “derivative” is a compound, usually organic obtained from another compound by a simple chemical process or an organic

compound containing a structural radical similar to that from which it is derived. Applicant has not provided what similar radicals are encompassed by the instant claim.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present is for the products, salts and stereoisomers.

The breadth of the claims

The breadth of the claims includes products, salts, derivatives, stereoisomers and solvates thereof.

The quantity of experimentation needed and the level of the skill in the art

The level of difficulty required to produce functional hydrates and solvates is extremely high. The level of skill in pharmacology/organic chemistry is also very high. However, despite such a high level of skill in the requisite art, the creation of solvates and hydrates is unpredictable to the extent that undue experimentation is required in order to make and use solvates and hydrates of the claimed compounds. There is an insufficient showing in the Specification, or the state of the art does not acknowledge that the solvates and hydrates of the claimed compounds can be created via routine experimentation.

Therefore, Applicant's Specification does not enable one of ordinary skill in the art to make and use the invention commensurate in scope with this claim.

Claims 13, 15 and newly added claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s)

contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of claims 13, 15, and newly added claims 16 and 17 include the use for the treatment of a variety of diseases such as the treatment of tumours, thromboembolic diseases and thrombosis. Furthermore, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming the intended use of therapy which includes the treatment of various diseases such as tumours.

Applicants claims are for the intended use of therapy such as the treatment of various tumours. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531) Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

Applicants newly added claims are directed to the treatment of thromboembolic disorders such as stroke, myocardial infarct, pulmonary embolism or deep venous thrombosis or artherosclerosis. Applicants' disclosure fails to enable the skilled artisan to use the compounds of the formula to treat any thromboembolic disorders.

The lack of predictability in the art of applicants' invention can be seen for example, in that it is the state of the art that data on the metabolism of factor Xa inhibitors has not been published yet (Hauptmann et al., page 223, 1449 page 6) and at the time of the publication, no published reports on the clinical use of factor Xa inhibitors existed. Furthermore, as seen in Kaiser (1449, page 6), Most of the specific factor Xa inhibitors known at the time of publication are still in the phase of preclinical development or are being investigated in first clinical studies, and while many treatment possibilities are discussed as possibilities, the real potential of factor Xa inhibitors has still to be validated in comprehensive clinical trials. Furthermore, an important point is that factor Xa inhibitors cannot interrupt thrombotic processes which are caused by generated thrombin. Page 432 of Kaiser states that Despite major progress in the development of antifactor Xa agents, there are still some unresolved issues such as that they are expected to be much less antithrombotically effective when sufficient amounts of thrombin have already been generated. Kaiser also discloses on page 433 that A particular factor Xa inhibitor might be useful for only a specific clinical indication, and it is likely that one drug might not be the optimum treatment for all thrombotic situations.

In regards to the treatment claimed the disorders embrace a vast array of problems, many of which are contradictory to others. It covers the thrombotic symptoms of diabetes, atherosclerosis and ischemic heart disease including congestive heart failure and myocardial infarction, stroke, and peripheral vascular disorders, such as deep-vein thrombosis, etc. Not one compound, let alone a genus of compounds, could possibly be effective against such disorders generally.

Stroke represents one of the most intractable medical challenges. Stroke is estimated to cause about 15% of deaths. Even those who survive normally suffer from persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy as so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, this trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatment, such as antiarrhythmics and antithrombotics don't get at the cause of the stroke or the damage caused, but are mostly done to insure adequate cardiac functioning.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the inhibition of factor Xa, one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability of the role of the inhibition of factor Xa

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the administration of the compounds of the claims one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability, for example, since it is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar

histopathological appearance can follow significantly different clinical courses and show different responses to therapy.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of diseases applicant considers as treatable on pages 4 and 5. In vitro data is discussed on page 21. However, the disclosure does not provide how the in vitro data correlates to the treatment of the assorted diseases claimed.

The uses covered by the claims are not enabled based solely on the assay testing reported in the specification. Various studies reported for compounds in clinical development rely on animal models and not simply assay testing as done herein. Note Hoffman V. Klaus 9 USPQ2d 1657 regarding the standard of testing that is necessary to establish the likelihood of in vivo use. Also see Ex parte Powers 220 USPQ 925. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of in vivo efficacy by those skilled in the art. See for example, In re Ruskin 148 USPQ 221; Ex parte Jovanovics 211 USPQ 907. Any evidence relied on by applicants must clearly show a reasonable expectation of in vivo success for any additional diseases that may still be embraced in response to this action. See MPEP 2164.05(a).

Additionally, for example, in regards to the treatment of specific cancers, in general, cell culture studies are not considered, in the cancer arts, to be reliably predictive of effects in cancer treatment, in vitro assays cannot easily assess host-tumor

and cell-cell interactions that may be important in the malignant state and cannot duplicate the complex conditions of in vivo therapy. This is because characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Those of skill in the art recognize that *in vitro* assays are useful to screen the effects of agents on cells. However, clinical correlations are generally lacking. The greatly increased complexity of the *in vivo* environment as compared with the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a simple extrapolation of *in vitro* assays to human therapeutic efficacy with any reasonable degree of predictability.

Further, there is no disclosure regarding how all types of diseases claimed having divers mechanisms are treated. Receptor activity is generally unpredictable and a highly structure specific area, and the data provided of is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is the use for the treatment of a variety of diseases and disorders.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of the multitude claimed would be benefited (treated) by the administration of the compound of the claims.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be

individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment of the various claimed diseases and disorders as a result necessitating one of skill to perform an exhaustive search for which disorders can be treated by what compounds of the instant claims in order to practice the claimed invention.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that “ a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to

engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday from 6:00am until 2:30pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Anderson/
Primary Examiner, AU 1626

21 December 2009

Rebecca Anderson
Primary Examiner
Art Unit 1626, Group 1620
Technology Center 1600